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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
FOLEY, SHANON A	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,933	CAO ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/21/2, 8/2/4*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Specification

The disclosure is objected to because of the following informalities: On page 2, line 27, the specification discusses the subject matter of "08/107/908". According to the information available from the PALM system within the Office, this application was issued as US 5,371,109 and the title of the patent is: Controlled Release Composition for a Biologically Active Material Dissolved or Dispersed in an L2-Phase. The patent does not mention BVD or N^{pro}. Therefore, it is presumed that the serial number described on page 2 of the disclosure contains a typo.

Appropriate correction is required.

Claim Objections

Claim 13 is objected to because of the following informalities: The claim has two periods at the end. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 9-29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 4 state that a mutated N^{pro} sequence comprises an intact 5' "region". It cannot be determined which portion of the 5' end is being referred to. This rejection also affects all dependent claims.

Claims 2, 3, 5, 6 and 7 recite "degenerate variants" of genomic sequences. However, the metes and bounds for what structural variations could be present in the genome, while still being recognizable as a BVDV genome cannot be determined. This rejection also affects all dependent claims.

Claim 6 is drawn to a nucleic acid molecule comprising a sequence "essentially as set forth in SEQ ID NO: 11". It cannot be determined which sequences are encompassed by this claim. This rejection also affects all dependent claims.

Claims 13 and 15 state that "a mutation into the 3' region of the N^{pro} protease gene". It cannot be determined what the boundaries of the "3' region" are. This rejection also affects all dependent claims.

Claim 14 recites, " about one third of the N^{pro} coding region from the 3' end". It is unclear what portion of the genome is intended.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 3, 5-7, 9-12 and 16-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The instant claims encompass "degenerative variants" of a BVDV nucleic acid sequence.

The metes and bounds for what structural variations could be present in the genome, while still being recognizable as a BVDV genome cannot be determined. The claims do not require that the nucleic acid sequences possess any particular distinguishing feature, biologic activity, or conserved structure. Therefore, the claims are drawn to an undefined genus of sequences.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, there is not even identification of any particular portion of the sequence that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of nucleic acids, given that the specification has only described SEQ ID NOs: 11 and 12. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention

and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleotides comprising the sequence set forth in SEQ ID NOs: 11 or 12, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that pBVDd6 is required to practice the claimed invention because it is a necessary limitation for the success of the invention as stated in the claim. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of ATCC NO: PTA-2532. See 37 CFR 1.802. One cannot practice the claimed invention

without the plasmid or determine whether a plasmid has the necessary characteristics without access to ATCC NO: PTA-2532. Therefore, access to ATCC NO: PTA-2532 is required to practice the invention. The specification does not provide a repeatable method for readily identifying characteristics associated with the plasmid and without access to it and it does not appear to be readily available material.

Deposit of pBVDd6 in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112., because the plasmid would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

Claims 1-7 and 9-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-7, 9-12 and 16-29 are drawn to an attenuated BVDV that has a mutated N^{pro} coding sequence within the genome. It is not clear from the claim language where in the genome the mutation is. However, the claims describe the attenuated virus as having a "5' region" of an N^{pro} that is intact and a monomeric bovine ubiquitin coding sequence that is between N^{pro} and the core protein. The claims also require that the genome is attenuated as a result of the described mutation. This asserted attenuation in the claims is required to be supported by some evidence in the specification that the recombinant viruses claimed possess the required characteristic. While the working examples in the disclosure teach how exemplary constructs are made and that the

resulting recombinant viruses have a slower growth rate that the parental wild-type virus, there is no indication or data presented that would indicate that the instant viruses are sufficiently attenuated to ameliorate or prevent viral infection. The prior art indicates that all cytopathic BVD strains comprise monomeric units of ubiquitin between N^{pro} and the core virus and that the presence of ubiquitin is a classical feature that distinguishes cytopathic BVD strains from non-cytopathic strains. See the teachings of Tautz e al. (Virology. 1993; 197: 74-85, especially Figure 1A) and Becher et al. (Journal of Virology. 1998; 72 (11): 8697-8704, especially Figure 3). Therefore, since the prior art indicates that the presence of ubiquitin is correlative to cytopathogenicity, the skilled artisan would not predict that the instant recombinant BVD virus(es) claimed would be sufficiently attenuated to treat and prevent BVD infection.

The claims also encompass "degenerate variants" of the instant BVD claimed. However, it cannot be determined what types of structural or functional mutations are required by the limitation recited. There is no working example or other teaching provided in the disclosure that shows a representative number of species encompassed by the genus claimed, or that the genus would be attenuated to treat and prevent BVD infection. The skilled artisan would also be unable to predict the structural or functional characteristics of the "degenerate variants".

Claims 13 and 15 are drawn to a method of modifying a wild-type BVDV by introducing a mutation into the 3' region of the N^{pro} gene that renders the N^{pro} protein inactive (emphasis added). The mutation recited in the claims is required to be singular, i.e. affecting a single nucleotide, to render the protein product inactive. However, the specification does not teach or provide a working example of a single mutation that could be made to the N^{pro} gene that would render the resulting protein inactive. The skilled artisan would be unable to predict which sort of

mutation, such as a substitution, deletion or addition, to which single nucleic acid within the N^{pro} gene would have the required result of an inactive N^{pro} protein. There is also no guidance provided in the disclosure that the single mutation introduced into the genome would result in the desired attenuated phenotype.

Claim 14 states that the mutation comprises a deletion of "about one third of the N^{pro} coding region from the 3' end". As discussed above, it cannot be determined which portion of the genome is intended to be deleted from the claim language and the skilled artisan would be unable to predict how much should be included in the recited deletion.

For these reasons, it is determined that an undue quantity of experimentation would be required of the skilled artisan to make or use the mutant BVD virus(es) claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by the sequence alignment of instant SEQ ID NO: 12 with GenEmbl database accession no: AF039181, submitted by Topliff et al. in Virology. 250 (1): 164-172 in 1998.

Claim 8 is drawn to a plasmid designated as a specific name associated with an ATCC deposit number, or alternatively, SEQ ID NO: 12. Since the sequence of Topliff et al. clearly

anticipate all of the structural features of instant SEQ ID NO: 12, the sequence of Topliff et al. clearly anticipate claim 8, see the sequence alignment provided.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (571) 272-0898. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shanon Foley
Patent Examiner, 1648